PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 04GN16E	**FOR FURTHER ACTION** See Form PCT/IPEA/416	
International application No. PCT/IT2004/000002	International filing date *(day/month/year)* 07.01.2004	Priority date *(day/month/year)* 10.01.2003
International Patent Classification (IPC) or national classification and IPC C07C259/10		
Applicant ITALFARMACO SPA et al.		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 5 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 3 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☒	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
06.08.2004	20.05.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Fitz, W Telephone No. +31 70 340-4359

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IT2004/000002

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-23 as originally filed

   Claims, Numbers

   1-17 received on 23.03.2005 with letter of 22.03.2005

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IT2004/000002

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-17
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	-

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following document:
D1: WO 97/43251 A

1.) The document D1 discloses anti-inflammatory hydroxamic acid derivatives. The compound of example 1 of D1 is structurally most closely related to the present compounds.
The compounds of present claim 1 differ from the compound of example 1 of D1 by the substituent on the phenyl group A.
The specific compounds recited in claim 10 are not disclosed in D1.
Accordingly, the subject-matter of claims 1-17 is new in the sense of Art. 33(2) PCT.

2.) Present compounds are structurally closely related to the compounds of D1. In the absence of a demonstrated surprising effect that is caused by a distinctive structural feature of the present compound over the structurally closest compound from D1, i.e. the compound of example 1 of D1 (wherein A is unsubstituted phenyl) the problem underlying the present application is seen as the provision of further anti-inflammatory hydroxamic acid derivatives.
The solution provided in the present application, e.g. adding certain substituent groups to the phenyl group, is an obvious measure that the skilled person, wishing to arrive at further compounds with the same biological activity, would take without having to rely on inventive activity.
Accordingly, the subject-matter of claims 1-17 does not involve an inventive step in the sense of Article 33(3) PCT.

3.) The subject-matter of claims 1-17 is industrially applicable, because the compounds are of pharmaceutical interest.

Re Item VI

Certain documents cited

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (SEPARATE SHEET)

International application No.
PCT/IT2004/000002

Certain published documents

Application No Patent No	Publication date *(day/month/year)*	Filing date *(day/month/year)*	Priority date *(valid claim)* *(day/month/year)*
WO03/013493	20.2.2003	26.7.2002	7.8.2001

Re Item VIII

Certain observations on the international application

1.) Although claims 1 and 10 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and/or in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.
Also, in contradiction with claim 1, claim 10 recites compounds which have unsubstituted phenyl and methylsulphanyl-substituted phenyl as the A group (i.e. the compounds of examples 2 and 8).

2.) Examples 2 and 8 do not fall under the scope of present claim 1, Art. 6 PCT.

3.) Dependent claim 4 renders claim 1 unclear, because in claim 4 A is defined as phenyl, whereas in main claim 1 A is defined as phenyl substituted with certain groups, Art. 6 PCT.

4.) In view of the present wording of claim 1, the dependent claims 5 and 8 appear to be superfluous and, consequently, render the claims inconcise, Art. 6 PCT.

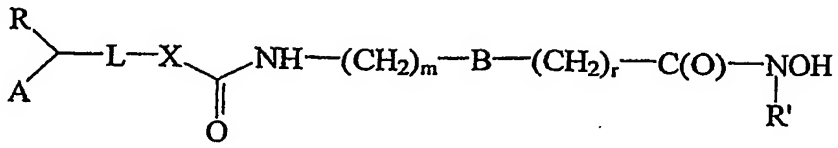
CLAIMS

EPO - DG 1

23. 03. 2005

(76)

1. Compounds of formula (I):



(I)

in which:

R is hydrogen, C_{1-4} alkyl or phenyl;

R' is hydrogen or C_{1-4} alkyl;

A is phenyl substituted with one or more groups selected from: alkoxy, nitro, perfluoroalkyl, phenoxy, phenyl, phenylalkoxy, benzoyloxy, and thioalkoxy;

L is a chain of from 1 to 5 carbon atoms optionally containing a double bond or an NR' group in which R' is as defined above, or it is absent;

X is absent;

r and m are, independently, 0, 1 or 2;

B is phenyl.

2. Compounds according to Claim 1 in which R is hydrogen.

3. Compounds according to Claim 1 in which R is methyl.

4. Compounds according to any one of Claims 1-3 in which A is phenyl.

5. Compounds according to any one of Claims 1-4 in which X is absent.

6. Compounds according to any one of Claims 1-5 in which L is methylene or ethylene.

7. Compounds according to any one of Claims 1-6 in which m and r are equal to zero.

8. Compounds according to any one of Claims 1-7 in which B is phenyl.

9. Compounds according to any one of Claims 1-8 in which R' is hydrogen.

10. A compound selected from:

N-hydroxy-4-[2-(4-trifluoromethyl-phenyl)-acetylamino]-

benzamide;
N-hydroxy-4-(3-phenyl-butyrylamino)-benzamide;
N-hydroxy-4-[3-(3-methoxy-phenyl)-propionylamino]-benzamide;
N-hydroxy-4-[2-(4-methoxy-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(4-ethoxy-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[3-(3,5-bis-trifluoromethyl-phenyl)-propionylamino]-benzamide;
N-hydroxy-4-[2-(3,4,5-trimethoxy-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(4-methylsulphanil-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(3-trifluoromethyl-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(3-nitro-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(3-phenoxy-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(diphenyl-4-yl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(2,3-dimethoxy-phenyl)-acetylamino]-benzamide;
2-[2-(4-hydroxycarbamoyl-phenylcarbamoyl)-ethyl]-phenyl ester of benzoic acid;
N-hydroxy-4-[2-(4-nitro-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(2-phenoxy-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(4,5-dimethoxy-2-nitro-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(2-benzyloxy-phenyl)-acetylamino]-benzamide;
N-hydroxy-4-[2-(2-nitro-phenyl)-acetylamino]-benzamide.

11. A compound according to claim 10 which is N-hydroxy-4-[2-(4-methoxy-phenyl)-acetylamino]-benzamide.

12. Compounds of any one of Claims 1-11 for use as medicaments.

13. Use of compounds of any one of Claims 1-11 for the preparation of medicaments with anti-inflammatory and/or auto-immune activity for the treatment of diseases such as spondyloarthropathy, rheumatoid arthritis, acute alcoholic hepatitis, inflammatory syndromes of the intestine (Crohn's disease and ulcerative colitis), asthma, diabetes, heart failure, intracerebral

haemorrhage, psoriasis, atopic dermatitis, contact dermatitis, glomerulonephritis, systemic lupus erythematosus, chronic pulmonary obstruction, pulmonary fibrosis, multiple sclerosis, sepsis, septic shock, etc.

14. Use of the compounds of any one of Claims 1-11 for the preparation of medicaments for the treatment of tumorous and/or neurodegenerative diseases.

15. Use of the compounds of any one of Claims 1-11 and at least one active ingredient with anti-tumour action for the preparation of medicaments for the treatment of tumorous and neurodegenerative diseases.

16. Pharmaceutical compositions containing the compounds of any one of Claims 1-11 mixed with suitable excipients and/or vehicles.

17. Pharmaceutical compositions containing the compounds of any one of Claims 1-11 and at least one active ingredient with anti-tumour action mixed with suitable excipients and/or vehicles.